Published in final edited form as:

Obstet Gynecol Clin North Am. 2014 December ; 41(4): 649–669. doi:10.1016/j.ogc.2014.08.007.

Current management and long-term outcomes following chorioamnionitis

Clark T. Johnson, MD, MPH^{1,3}, Azadeh Farzin, MD^{2,3,4}, and Irina Burd, MD, PhD^{1,3,5,*}

¹Department of Gynecology and Obstetrics, Johns Hopkins Medical Institutions, Baltimore, Maryland 21287

²Department of Pediatrics, Johns Hopkins Medical Institutions, Baltimore, Maryland 21287

³Integrated Research Center for Fetal Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland 21287

⁴International Center for Maternal & Newborn Health, Johns Hopkins University, Baltimore, Maryland 21287

⁵Department of Neurology, Johns Hopkins Medical Institutions, Baltimore, Maryland 21287

Keywords

chorioamnionitis; neonatal Sepsis; endomyometritis; fetal infection; fetal inflammation; perinatal infection; perinatal inflammation; funisitis

Introduction

Chorioamnionitis is defined as the presence of active infection in the amniotic sac that causes inflammatory changes in the mother. Strict diagnosis of chorioamnionitis in the absence of invasive testing is problematic due to a lack of consistency. Multiple signs and symptoms are consistent with chorioamnionitis, diagnosed prior to delivery, and as a result, diagnostic criteria may vary by provider and institution. Therefore, the quantification of the burden of disease of chorioamnionitis is significantly challenging.

Chorioamnionitis is traditionally considered to be a polymicrobial process, although there is evidence to suggest that bacterial proliferation may not be the initiating event to cause chorioamnionitis¹. Notably, many of the associated bacteria tend to colonize amniotic fluid with low virulence². It is unclear what causes these bacteria to transition from colonizers to pathologic contributors and, eventually, to chorioamnionitis³. *Mycoplasma*, in particular,

© 2014 Elsevier Inc. All rights reserved

*Corresponding author: Irina Burd, MD, PhD, iburd@jhmi.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The authors have nothing to disclose

seems to commonly colonize the reproductive tract and can be associated with adverse pregnancy outcomes in certain circumstances.⁴

Maternal complications of chorioamnionitis are primarily short-term, including postpartum hemorrhage, wound infection and endomyometritis. Pregnancy complications, including preterm labor and delivery, add to the significant burden of disease. Chorioamnionitis in one pregnancy can influence the risk of recurrence in a future pregnancy, although this risk remains low. Obstetrical history of delivering a child with Group B Streptococcus (GBS sepsis) early onset neonatal sepsis is an indication for routine GBS prophylaxis in labor for all future pregnancies.

GBS infections, historically, has been a significant contributor to the burden of disease of chorioamnionitis. Recent policies of screening and prophylaxis in labor have been able to significantly decrease its associated morbidity. Despite aggressive GBS prophylaxis, rates of intrauterine infection and associated morbidity remain high.

Chorioamnionitis is associated with many short-term and long-term neonatal complications. In cases of preterm birth, the child's risk cerebral palsy, brain injury and necrotizing enterocolitis are compounded by associated increased risk of prematurity.

Disease description

Chorioamnionitis diagnosis varies widely across different institutions and countries, with implications both for treatment protocols and for clinical studies. Fever is commonly used in addition to two of the signs from the table to make a diagnosis for study inclusion⁵. (**Box 1**) In clinical practice, diagnostic criteria can vary more widely. Clinically, the presence of intrapartum fever warrants attention. With improved clinical outcomes following antibiotic use, the threshold for clinical diagnosis and treatment can be lower than that for inclusion in clinical studies. Fever is the most predictive clinical sign that correlate to pathology, although the presence of other signs are used to make a diagnosis due to the imperfect specificity of fever in diagnosis of chorioamnionitis⁵.

Box 1

Signs and symptoms for diagnosis of chorioamnionitis
Fever >100.4 F
Uterine Tenderness
Maternal Tachycardia
Fetal Tachycardia
Purulent amniotic fluid

There does appear to be a relationship between regional anesthesia and fever, which may confound evaluation of relationships. Increased pyrexia is known to be associated with epidural use⁶. Given the relative importance of fever in the diagnosis of clinical chorioamnionitis, it is not surprising that epidural use and an associated fever may have a

confounding effect on clinical diagnosis of chorioamnionitis⁷. It is these types of confounding relationships affecting clinical diagnosis that make externally consistent diagnosis of chorioamnionitis challenging.

Chorioamnionitis is a global disease, further complicating its assessment⁸. A wide variety of resources across countries can affect diagnosis and treatment in a particular area, contributing to disparities in the burden of disease. Given widely variable diagnosis and reporting of the condition, and as well as prevalence of confounding factors such as epidural anesthesia, it becomes challenging to draw firm conclusions about the global epidemiology of clinical chorioamnionitis.

Amniotic fluid sampling and culture can be used in the diagnosis of chorioamnionitis⁹. Unfortunately, due to the invasive nature of the procedure, its widespread use is limited. Culture of the fluid may be an objective assessment of the presence of chorioamnionitis, but clinical utility is limited by the time needed to obtain results as well as the potential colonization of the amniotic fluid without affecting an inflammatory response.

Histopathologic diagnosis is considered to be the gold-standard by some, as it avoids some of the subjectivity of clinical diagnosis⁵. Unfortunately, these data may not be available until after delivery, limiting its clinical utility. Clinical scenarios occur where a neonate may be discharged from the hospital and clinically well, with a pathologic evaluation of the placenta that demonstrates evidence of chorioamnionitis. Given the high prevalence of histopathologic chorioamnionitis in asymptomatic neonates, this finding may not affect clinical treatment by itself, but may be useful in the presence of other clinical signs¹⁰. This diagnosis may ultimately be of limited importance as an isolated finding in regards to the clinical management of the neonate¹¹.

Even within histopathologic diagnosis, multiple criteria exist. Diagnosis of histologic chorioamnionitis is based on the presence of acute changes within the amnion and chorion⁹. Similarly, funisitis involves acute inflammation within the umbilical cord. Diagnosis can be made with the presence of either or both of these findings. Similar to clinical chorioamnionitis, histopathologic diagnosis is challenged by variability among pathologists in reaching a shared diagnosis on a single specimen¹².

Histopathologic chorioamnionitis has been reported to be one-fourth of term deliveries¹³. In general, it appears that histologic chorioamnionitis is more common than clinically evident chorioamnionitis, at term or otherwise⁹.

There appears to be correlation between histologic chorioamnionitis and maternal symptoms, such as fever⁵. Additionally, there appears to be a relationship between severe histopathologic findings and placental abruption¹⁴. A recent study has suggests that acute histopathologic chorioamnionitis at term is usually a result of a non-infectious inflammatory process¹⁵. The idea that a large number of studies evaluating chorioamnionitis and outcomes are actually based on a diagnosis that is mostly related to a non-infectious process frustrates comprehensive conclusions.

Chorioamnionitis, whether it is diagnosed histopathologically or clinically, leads to the fetal immune response syndrome (FIRS)¹⁶. **(Figure 1)** Animal studies have shown that preterm and term neonates may have subtle systemic responses to chorioamnionitis, but that these responses may lead to significant long-term¹⁷⁻¹⁹.

Risk Factors

There are multiple known risk factors associated with chorioamnionitis. Risk factors are demonstrated in Box 2, which is then followed by Box 3 outline bacteria that are commonly isolated from and associated with cases of chorioamnionitis

Box 2

A list of reported risk factors for the development of chorioamnionitis

Obstetric Risk Factors for Chorioamnionitis
Prolonged Labor
Prolonged Rupture of Membranes (PROM)
Prolonged Labor
Nulliparity
History of chorioamnionitis in prior pregnancy
Group B Streptococcus Colonization
Bacterial Vaginosis
Sexually Transmitted Diseases
Other Genital Tract infection
Meconium stained fluid
Multiple digital examinations
Fetal Scalp Electrodes (FSEs)
Intrauterine Pressure Catheters
Epidural Anesthesia
Tobacco Use
Alcohol Use

Box 3

Bacteria that are commonly isolated from and associated with cases of chorioamnionitis

Bacteria Commonly Isolated from Cases of Chorioamnionitis
Mycoplasma
Enterobacteriaceae
Group B Streptococcus
Staphylococcus Aureus

Gardnerella vaginalis
Neisseria gonorrhoeae
Chlamydia trachomatis

Neonates are at particular risk for sequelae from chorioamnionitis if they are already compromised at the time of delivery. Specific risk factors are listed in Box 4, below.

Box 4

Underlying neonatal risk factors for potential sequelae following chorioamnionitis

Neonatal Risk Factors for Exacerbation from Chorioamnionitis
Genetic anomalies
Acidemia
Delayed antibiotic administration
Prematurity

Prevalence/Incidence/Mortality Rate

Clinical chorioamnionitis is estimated to affect 1-4% of pregnancies worldwide in developed countries⁹. Data is lacking in developing nations, but is likely higher than this rate. Maternal bacteremia occurs in 5-10 % of women with chorioamnionitis⁹.

The percentage of neonatal deaths attributable to chorioamnionitis is difficult to quantify due to the fact that the mechanism of injury is due to causing significant morbidity, which in turn causes death. The true burden of disease is reflected further when discussing neonatal outcomes.

Similarly, maternal morbidity directly related to chorioamnionitis is difficult to assess. Chorioamnionitis is associated with many obstetric complications that can lead to death, but assessing the precise attribution of chorioamnionitis remains challenging.

GBS

GBS was the leading cause of neonatal sepsis in the 1970s in the US¹⁴ (**Figure 2**). The next decades saw the development of effective treatment of maternal carriers with IV antibiotics, penicillin or otherwise if allergic. Thereafter, the development of standardized screening testing during pregnancy led to universal screening (**Figure 3**), as recommended by the professional organizations. With the development of consensus guidelines (**Figure 4**), this led to the dramatic reduction of neonates affected by GBS that is seen today.

Across different countries, GBS colonization rates vary⁸. However, there is additional evidence that portions of Africa are at similar colonization rates⁸. The Far East has lower

reported rates, but this could be due to methodological issues in screening for and reporting GBS colonization⁸. There are significant challenges in assessing GBS prevalence in developing countries and its associated burden of disease to help establish differences in GBS epidemiology in the global arena⁸.

Clinical Outcomes

Many adverse maternal outcomes are significantly associated with chorioamnionitis (**Box 5**); however, many of these outcomes do not appear to be related to the duration of infection, rather, simply, to its presence²⁰.

Box 5

Potential maternal obstetric sequelae associated with chorioamnionitis

Sequelae of Chorioamnionitis
Maternal
Dysfunctional Labor
Increased Cesarean Delivery Risk
Postpartum Hemorrhage
Blood Transfusion
Postpartum infection

Neonates affected by chorioamnionitis can have significant sequelae (**Box 6**).

Box 6

Potential neonatal sequelae associated with chorioamnionitis

Neonatal
Sepsis
Pneumonia
Respiratory distress
Asphyxia
Necrotizing enterocolitis
Intraventricular hemorrhage
Periventricular leukomalacia
Cerebral Palsy
Long term neuro-developmental delay
Death

Chorioamnionitis has both short-term and long-term complications for the neonate. Cerebral palsy and many of these outcomes are linked to both histology²¹⁻²⁶ and clinical diagnosis²⁷⁻³⁰. One of the challenges in assessing the influence of chorioamnionitis on clinical neonatal outcomes is the different diagnostic criteria used in different studies.

Interestingly, when controlling for major morbidity associated with chorioamnionitis, there does not appear to be an independent relationship between chorioamnionitis and death²⁸. With that, any association between chorioamnionitis and death is likely to be mediated through the significant morbidity that it causes.

Chorioamnionitis is clearly associated with an increased risk of a range of morbidities as noted in Table 1. Interestingly, while chorioamnionitis appears to be associated with an increased risk of early onset sepsis as would be expected, there is a decreased risk of late onset sepsis³¹. It is postulated that the mechanisms of this developed resistance is related to an enhanced immune response, following the inflammatory event at birth that may help to protect the neonate³¹. See Table 2 for representative studies or meta-analyses evaluating the relationship between chorioamnionitis and selected short term neonatal outcomes.

Management – Preventive and Therapeutic Options

As discussed, one of the major challenges for treatment of chorioamnionitis is the imperfect sensitivity and specificity of clinical diagnoses. Previous studies have looked at the use of antibiotics in different populations at high risk for chorioamnionitis with mixed results³⁷⁻³⁹. Currently, it is not recommended to treat patients at-risk for chorioamnionitis, but rather reserve treatment for when clinical chorioamnionitis is diagnosed, based on a variety of criteria⁴⁰. Excessive use of antibiotics in this setting is associated with inferior neonatal outcomes^{41,42}. This is consistent with the relationship of prolonged empiric antibiotics administered to neonates being associated with increased morbidity⁴³. Antibiotics have been specifically studied in preterm labor with intact membranes without clinical benefit⁴⁴. Specific study evaluating the use of empiric Flagyl and Erythromycin did not appear to reduce histologic chorioamnionitis⁴⁵.

Antibiotics for Chorioamnionitis

IV antibiotics are generally considered to be the preferred treatment for chorioamnionitis where available. Limited studies have suggested the non-superiority of specific broad spectrum regimens, including a combination of ampicillin, gentamycin, and clindamycin, or single agent piperacillin-tazobactam. Oral options may be considered in areas where IV antibiotics are not available, although there is evidence that oral antibiotic therapy with clindamycin does not seem to significantly reduce the rate of histologic chorioamnionitis⁴⁷. If considered, broad spectrum regimens including penicillins or cephalosporins and a macrolide antibiotics would be prudent. This can be a particular issue in the global arena as a result of the absence of a variety of antibiotic regimens.

Preterm premature rupture of membranes has been well studied. Management with two days of IV antibiotics followed by five days of oral antibiotics are associated with increasing the latency between PPRM and Delivery^{48,49}. Further use of antibiotics beyond this timeline appears to be associated with worse neonatal outcomes without apparent clinical benefit⁴⁰.

The prophylaxis protocol for GBS colonization in labor has been well defined in the United States^{50,51}. Consideration for prophylaxis should be considered in the clinical circumstances as noted. Prophylaxis is indicated at the time of induction or labor. Penicillin therapy is

preferred due to the very low level of resistance among GBS isolates. In patients with allergy or other contraindication, therapy can be considered as indicated in Table 3.

With a diagnosis of chorioamnionitis, delivery should be considered (**Figure 5**). While antibiotic therapy with the fetus *in utero* may temporize sequelae of chorioamnionitis, extended latency can lead to maternal sepsis with significant morbidity and mortality and is not recommended. Immediate delivery by cesarean is also not indicated. Frequently, non-reassuring fetal status or fetal tachycardia will improve with a combination of anti-pyretics and antibiotics. Unless contraindicated, induction and trial of labor can and should be undertaken. There is not evidence to suggest that prolongation of a pregnancy complicated by chorioamnionitis leads to worse maternal or neonatal outcomes.

Neonatal management following delivery of chorioamnionitis is to provide secondary prevention against neonatal sepsis and infectious sequelae. Strict surveillance with indicated use of antibiotic and supportive therapy can help avert significant morbidity. Suggested management for the neonate delivered from a GBS positive mother is shown in Figure 4. This algorithm can be similarly adapted to evaluate neonates following delivery affected by chorioamnionitis to help limit morbidity.

Neonatal Management

Box 7

A list of potential diagnostic criteria to evaluate the neonate at risk for sepsis

Neonatal Sepsis Evaluation
-Blood culture
-CBC/platelets
-White blood cell differential
-Chest XRay
-Lumbar Puncture

Prompt diagnosis (Box 7) of the neonate suspected to be septic should be treated promptly to help avert short and long term morbidity. Treatment is composed primarily of broad spectrum antibiotics, with a penicillin to cover GBS and *Listeria monocytogenes* and gentamicin to cover *E. Coli* and local gram negative bacteria. Supportive care should be employed, and evaluation for evidence of infection of a particular organ system can guide further antibiotic management (**Figure 6**).

Complications and Concerns

Screening for GBS is imperfect and technically challenging to employ 100% compliance in any population. As such, there remain potential risks of undertreatment in the population and the risk of preventable morbidity. Ultimately, as worldwide effort to better screen and treat GBS, there will be diminishing returns on efforts that limit eradication of morbidity⁵².

Studies to develop and implement a vaccine against GBS to be used in the general population have the potential to overcome the limits in the current approach to GBS and prevent morbidity⁴.

Just as screening and treatment for GBS is ultimately imperfect in implementation, there are significant challenges with systematic screening and treatment for chorioamnionitis across the population. Survey of obstetric practice reveals a wide spectrum of clinical criteria for diagnosis as well as approach to treatment of chorioamnionitis⁵³. Until a uniform diagnostic criterion for chorioamnionitis and women at risk for resultant morbidity can be implemented, challenges in optimizing maternal and neonatal morbidity from chorioamnionitis will be limited. Further efforts to develop better criteria to diagnose and treat chorioamnionitis will help reduce morbidity⁵⁴.

It is the unfortunate reality that chorioamnionitis is a significant risk factor for preterm labor and delivery. Retrospective studies must consider this relationship when evaluating the association with morbidity, as preterm delivery itself is an independent risk factor for many of the morbidities that are associated with chorioamnionitis, and without careful analysis can overestimate the association of chorioamnionitis with various morbidities^{33,34}. A result of this relationship between chorioamnionitis and preterm delivery is a synergistic exacerbation of neonatal morbidity, further incentivizing the importance of diagnosis and treatment of chorioamnionitis⁵⁵.

Betamethasone is well established as an important tool in the prevention of neonatal morbidity resulting from preterm delivery⁵⁶. One might question the utility of immune suppressing steroids in the setting of chorioamnionitis, out of concern that it might exacerbate infection and neonatal outcome⁵⁷. Meta-analysis of human studies has demonstrated that steroid administration in the setting of prematurity and chorioamnionitis is associated improved neonatal outcomes among a variety of potential morbidities⁵⁸. Chorioamnionitis is not a contraindication to administering steroids to optimize neonatal outcome of the premature fetus⁵⁶. Efforts should be made to ensure this important intervention is not withheld from preterm pregnancies with chorioamnionitis, lest a significant benefit be withheld from this high risk population.

Chorioamnionitis is a global disease. While efforts at improving screening and preventing morbidity have been successful in developed countries with much effort and investment⁵⁹, little progress has been made in the global arena. Efforts to consider international issues in implementing effective screening and treatment strategies will be needed to prevent future morbidity. Efforts to develop a GBS vaccine and implement in the global arena is an example of successful efforts to bridge this gap⁶⁰. Future efforts to focus on improving screening and potential for available treatments for chorioamnionitis in a variety of settings will be needed to optimize maternal and neonatal outcomes worldwide.

Summary/Discussion/Future pathways

Discussion of chorioamnionitis has been focused on clinical or histopathologic chorioamnionitis. Amniotic and intrauterine colonization without evidence of inflammation warrants attention⁶¹. Within chorioamnionitis, the presence of *in utero* inflammation appears

to significantly exacerbate neonatal outcomes, as opposed to chorioamnionitis without evidence of inflammation⁶². Colonization is seen in amniocentesis samples that grow organisms but without elevated inflammatory markers such as Interleukin-6⁶¹. Care in interpretation may need to be taken, depending on the colonized organism, specifically some mycoplasma that might have increased pathogenicity and potential to induce morbidity^{63,64}.

A discussion of “asymptomatic” colonization draws attention to the contrapositive: aseptic amniotic fluid with elevated inflammatory markers (such as IL-6), which may share outcomes as a patient with diagnosed chorioamnionitis⁶¹. Recent studies have demonstrated this clinical entity, and its management has yet to be established and optimized. Antibiotics would be of limited utility, as the consequences appear to result from inflammation rather than infection, and future research will point in this direction to develop effective treatment.

While much work has been done into inflammatory markers and their association with preterm labor, PPROM, and neonatal compromise, however few studies have been able to demonstrate clinical benefit from their use⁶⁵. One aspect of this challenge is detecting inflammatory markers in a non-invasive manner, to limit risks that may outweigh the potential benefits of the information. In addition, future efforts will have to evaluate treatment modalities, antibiotics or inflammatory modulating drugs that may help improve outcomes. These studies are urgently needed.

Multiple animal models exist for the study of inflammation and chorioamnionitis¹⁷⁻¹⁹. Models exist in mice, rats, and rabbits using various infectious organisms and lipopolysaccharide, that have developed damage to various areas of the brain (white matter and gray matter) as well as behavioral changes¹⁷⁻¹⁹. These models, and future models that build on these discoveries, hold much promise for the future studies of chorioamnionitis, inflammation, and their effect on long-term sequelae.

The role of chorioamnionitis in preterm labor is significant, as a majority of preterm deliveries can be attributed to evidence of chorioamnionitis, clinical or pathologic. Future studies evaluating populations with differential risks of preterm labor (e.g. multiple gestations, history of prior preterm delivery, and various ethnic minorities) may lead to a better understanding of the contribution of chorioamnionitis to preterm labor and delivery in these populations. As it is likely that the fraction of these deliveries attributed to chorioamnionitis or infection would vary among the different groups, insight may be gained in the further evaluation of these differences.

Efforts at developing a maternal vaccine are well underway. Antepartum treatment appears to confer neonatal protection⁶⁶. The burden of GBS remains, particularly with late-onset GBS sepsis, which isn't necessarily treated with current screening regimens⁶⁷. Some of this morbidity may be due to GBS transmission during breastfeeding⁶⁸. Implementation of a to-be-developed vaccine may even further reduce the horrific morbidity of preventable neonatal sepsis⁶⁷. Studies have evaluated its cost-effectiveness in South Africa, and found that implementation of a vaccine would likely be cost-effective and a worthwhile process⁵⁹. In addition, it appears that such a vaccine would be well accepted by an American

population⁶⁹. In sum, the vaccination would help reduce preventable morbidity in developed and developing countries^{60,70}.

Future directions of management will rely on more specific diagnoses of chorioamnionitis^{54, 71}. Efforts to develop more rapid evaluation of amniocentesis samples have the potential to provide a rapid and accurate diagnostic test to guide clinical management^{72, 73}. Optimization of treatment will rely on further delineation of phenotypes of the clinical scenarios, determination and screening for biomarkers as proxies for risk, effective development of significant biochemical pathways, determination of environmental influences on these models, as well as elucidation of the influence of racial and ethnic factors on these pathways⁷¹. Future interventions will rely on a customization of these factors to best establish an individual's risk in order to implement therapies that are optimized for the individual. Empiric therapy for suspected cases remains the standard of care until that time.

References

*Indicates meta-analysis

1. Kim MJ, Romero R, Gervasi MT, Kim JS, Yoo W, Lee DC, Mittal P, et al. Widespread microbial invasion of the chorioamniotic membranes is a consequence and not a cause of intra-amniotic infection. *Laboratory Investigation; a Journal of Technical Methods and Pathology*. 2009; 89(8): 924–36. 2009. Aug.
2. Keski-Nisula L, Kirkinen P, Katila ML, Ollikainen M, Saarikoski S. Cesarean delivery. Microbial colonization in amniotic fluid. *Journal of Reproductive Medicine*. Feb; 1997 42(2):91–8. [PubMed: 9058344]
3. Combs CA, Gravett M, Garite TJ, Hickok DE, Lapidus J, Porreco R, Rael J, Grove T, Morgan TK, Clewell W, Miller H, Luthy D, Pereira L, Nageotte M, Robilio PA, Fortunato S, Simhan H, Baxter JK, Amon E, Franco A, Trofatter K, Heyborne K, ProteoGenix/Obstetrix Collaborative Research Network. Amniotic fluid infection, inflammation, and colonization in preterm labor with intact membranes. *American Journal of Obstetrics and Gynecology*. Feb; 2014 210(2):125.e1–125.e15. [PubMed: 24274987]
4. Schrag SJ, Verani JR. Intrapartum antibiotic prophylaxis for the prevention of perinatal group B streptococcal disease: experience in the United States and implications for a potential group B streptococcal vaccine. *Vaccine*. Aug 28; 2013 31(Suppl 4):D20–6. [PubMed: 23219695]
5. Curtin WM, Katzman PJ, Florescue H, Metlay LA. Accuracy of signs of clinical chorioamnionitis in the term parturient. *Journal of Perinatology*. 2013; 33(6):422–8. Jun. [PubMed: 23154669]
6. Fusi L, Steer PJ, Maresh MJ, Beard RW. Maternal pyrexia associated with the use of epidural analgesia in labour. *Lancet*. Jun 3; 1989 1(8649):1250–2. [PubMed: 2566791]
7. Abramovici A, Szychowski JM, Biggio JR, Sakawi Y, Andrews WW, Tita AT. Epidural Use and Clinical Chorioamnionitis among Women Who Delivered Vaginally. *American Journal of Perinatology*. Apr 4.2014 Epub ahead of print.
8. Le Doare K, Heath PT. An overview of global GBS epidemiology. *Vaccine*. 2013; 31(Suppl 4):D7–12. Aug 28. [PubMed: 23973349]
9. AT, Tita; Andrews, WW. Diagnosis and management of clinical chorioamnionitis. *Clinics in Perinatology*. Jun; 2010 37(2):339–54. [PubMed: 20569811]
10. Hoang D, Charlagorla P, Salafia C, VanHorn S, Dygulska B, Narula P, Gad A. Histologic chorioamnionitis as a consideration in the management of newborns of febrile mothers. *The Journal of Maternal-Fetal and Neonatal Medicine*. 2013; 26(8):828–32. May. [PubMed: 23211126]
11. Torricelli M, Voltolini C, Conti N, Vellucci FL, Orlandini C, Bocchi C, Severi FM, Toti P, Buonocore G, Petraglia F. Histologic chorioamnionitis at term: implications for the progress of

- labor and neonatal wellbeing. *Journal of Maternal-Fetal and Neonatal Medicine*. Jan; 2013 26(2): 188–92. [PubMed: 22928534]
12. Sun CC, Revell VO, Belli AJ, Viscardi RM. Discrepancy in pathologic diagnosis of placental lesions. *Archives of Pathology and Laboratory Medicine*. Jun; 2002 126(6):706–9. [PubMed: 12033960]
 13. Mi Lee S, Romero R, Lee KA, Jin Yang H, Joon Oh K, Park CW, Yoon BH. The frequency and risk factors of funisitis and histologic chorioamnionitis in pregnant women at term who delivered after the spontaneous onset of labor. *Journal of Maternal-Fetal and Neonatal Medicine*. Jan; 2011 24(1):37–42. [PubMed: 20698737]
 14. Nath CA, Ananth CV, Smulian JC, Shen-Schwarz S, Kaminsky L, New Jersey-Placental Abruption Study Investigators. Histologic evidence of inflammation and risk of placental abruption. *American Journal of Obstetrics and Gynecology*. 2007; 197(3):319.e1–e6. Sep. [PubMed: 17826437]
 15. Roberts DJ, Celi AC, Riley LE, Onderdonk AB, Boyd TK, Johnson LC, Lieberman E. Acute histologic chorioamnionitis at term: Nearly always noninfectious. *PloS One*. 2012; 7(3):e318–19.
 16. Kallapur SG, Presicce P, Rueda CM, Jobe AH, Choungnet CA. Fetal immune response to chorioamnionitis. *Seminars in Reproductive Medicine*. 2014; 32(1):56–67. Jan. [PubMed: 24390922]
 17. Burd I, Balakrishnan B, Kannan S. Models of fetal brain injury, intrauterine inflammation, and preterm birth. *American Journal of Reproductive Immunology*. 2012; 67(4):287–94. Apr. [PubMed: 22380481]
 18. Dada T, Rosenzweig JM, Al Shammary M, Firdaus W, Al Rebh S, Borbiev T, Tekes A, Zhang J, Alqahtani E, Mori S, Pletnikov MV, Johnston MV, Burd I. Mouse model of intrauterine inflammation: Sex-specific differences in long-term neurologic and immune sequelae. *Brain, Behavior and Immunity*. May. 2014 38:142–50.
 19. Kannan S, Dai H, Navath RS, Balakrishnan B, Jyoti A, Janisse J, Romero R, Kannan RM. Dendrimer-based postnatal therapy for neuroinflammation and cerebral palsy in a rabbit model. *Science Translational Medicine*. Apr 18; 2012 4(130):130–46.
 20. Rouse DJ, Landon M, Leveno KJ, Leindecker S, Varner MW, Caritis SN, O'Sullivan MJ, et al. National Institute of Child Health And Human Development, Maternal-Fetal Medicine Units Network. The Maternal-Fetal Medicine Units cesarean registry: chorioamnionitis at term and its duration-relationship to outcomes. *American Journal of Obstetrics and Gynecology*. 2004; 191:211–216. [PubMed: 15295368]
 21. Salas AA, Faye-Petersen OM, Sims B, Peralta-Carcelen M, Reilly SD, McGwin G Jr, Carlo WA, Ambalavanan N. Histological characteristics of the fetal inflammatory response associated with neurodevelopmental impairment and death in extremely preterm infants. *The Journal of Pediatrics*. 2013; 163(3):652. Sep. 7.e1-2. [PubMed: 23664630]
 22. van Vliet EO, de Kieviet JF, van der Voorn JP, Been JV, Oosterlaan J, van Elburg RM. Placental pathology and long-term neurodevelopment of very preterm infants. *American Journal of Obstetrics and Gynecology*. 2012; 206(6):489.e1–7. Jun. [PubMed: 22521456]
 23. Suppiej A, Franzoi M, Vedovato S, Marucco A, Chiarelli S, Zanardo V. Neurodevelopmental outcome in preterm histological chorioamnionitis. *Early Human Development*. 2009; 85(3):187–9. Mar. [PubMed: 18996654]
 24. Soraisham AS, Trevenen C, Wood S, Singhal N, Sauve R. Histological chorioamnionitis and neurodevelopmental outcome in preterm infants. *Journal of Perinatology*. 2013; 33(1):70–5. Jan. [PubMed: 22555781]
 25. Rovira N, Alarcon A, Iriondo M, Ibañez M, Poo P, Cusi V, Agut T, Perterra A, Krauel X. Impact of histological chorioamnionitis, funisitis and clinical chorioamnionitis on neurodevelopmental outcome of preterm infants. *Early Human Development*. Apr; 2011 87(4):253–7. [PubMed: 21354722]
 26. Perrone S, Toti P, Toti MS, Badii S, Becucci E, Gatti MG, Marzocchi B, Picardi A, Buonocore G. Perinatal outcome and placental histological characteristics: A single-center study. *The Journal of Maternal-Fetal and Neonatal Medicine*. Apr; 2012 25(Suppl 1):110–3. [PubMed: 22348288]

27. Shatrov JG, Birch SC, Lam LT, Quinlivan JA, McIntyre S, Mendz GL. Chorioamnionitis and cerebral palsy: A meta-analysis. *Obstetrics and Gynecology*. 2010; 116(2):387–92. *. Pt 1. Aug. [PubMed: 20664400]
28. García-Muñoz Rodrigo F, Galán Henríquez GM, Ospina CG. Morbidity and Mortality among Very-Low-Birth-Weight Infants Born to Mothers with Clinical Chorioamnionitis. *Pediatrics and Neonatology*. Apr 15.2014 Epub ahead of print.
29. Alexander JM, Gilstrap LC, Cox SM, McIntire DM, Leveno KJ. Clinical chorioamnionitis and the prognosis for very low birth weight infants. *Obstetrics and Gynecology*. 1998; 91(5):725–9. Pt 1. [PubMed: 9572219]
30. Wu YW, Colford JM Jr. Chorioamnionitis as a risk factor for cerebral palsy: A meta-analysis. *JAMA*. Sep 20; 2000 284(11):1417–24. *. [PubMed: 10989405]
31. Strunk T, Doherty D, Jacques A, Simmer K, Richmond P, Kohan R, Charles A, Burgner D. Histologic chorioamnionitis is associated with reduced risk of late-onset sepsis in preterm infants. *Pediatrics*. Jan; 2012 129(1):e134–41. [PubMed: 22157134]
32. Been JV, Lievense S, Zimmermann LJ, Kramer BW, Wolfs TG. Chorioamnionitis as a risk factor for necrotizing enterocolitis: a systematic review and meta-analysis. *Journal of Pediatrics*. Feb; 2013 162(2):236–42. *. e2. [PubMed: 22920508]
33. Hartling L, Liang Y, Lacaze-Masmonite T. Chorioamnionitis as a risk factor for bronchopulmonary dysplasia: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed*. Jan; 2012 97(1):F8–F17. *. [PubMed: 21697236]
34. Mitra S, Aune D, Speer CP, Saugstad OD. Chorioamnionitis as a risk factor for retinopathy of prematurity: a systematic review and meta-analysis. *Neonatology*. 2014; 105(3):189–99. *. [PubMed: 24481268]
35. Pappas A, Kendrick DE, Shankaran S, Stoll BJ, Bell EF, Laptook AR, Walsh MC, et al. Chorioamnionitis and early childhood outcomes among extremely low-gestational-age neonates. *JAMA Pediatrics*. Feb; 2014 168(2):137–47. [PubMed: 24378638]
36. Rovira N, Alarcon A, Iriondo M, Ibanez M, Poo P, Cusi V, Agut T, Pertierra A, Krauel X. Impact of histological chorioamnionitis, funisitis and clinical chorioamnionitis on neurodevelopmental outcome of preterm infants. *Early Human Development*. 87(4):253–7. 2011. Apr. [PubMed: 21354722]
37. Nabhan AF, Elhelaly A, Elkadi M. Antibiotic prophylaxis in prelabor spontaneous rupture of fetal membranes at or beyond 36 weeks of pregnancy. *International Journal of Gynaecology and Obstetrics*. Jan; 2014 124(1):59–62. [PubMed: 24140220]
38. Ovalle A, Romero R, Gómez R, Martínez MA, Nien JK, Ferrand P, Aspillaga C, Figueroa J. Antibiotic administration to patients with preterm labor and intact membranes: is there a beneficial effect in patients with endocervical inflammation? *Journal of Maternal-Fetal and Neonatal Medicine*. Aug; 2006 19(8):453–64. [PubMed: 16966109]
39. Hutzal CE, Boyle EM, Kenyon SL, Nash JV, Winsor S, Taylor DJ, Kirpalani H. Use of antibiotics for the treatment of preterm parturition and prevention of neonatal morbidity: a metaanalysis. *American Journal of Obstetrics and Gynecology*. Dec; 2008 199(6):620.e1–8. *. [PubMed: 18973872]
40. ACOG (American Congress of Obstetricians and Gynecologists) Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 120: Use of Prophylactic Antibiotics in Labor and Delivery. *Obstetrics and Gynecology*. Jun; 2011 117(6):1472–83. [PubMed: 21606770]
41. Didier C, Streicher MP, Chognot D, Campagni R, Schnebelen A, Messer J, Donato L, Langer B, Meyer N, Astruc D, Kuhn P. Late-onset neonatal infections: incidences and pathogens in the era of antenatal antibiotics. *European Journal of Pediatrics*. Apr; 2012 171(4):681–7. [PubMed: 22134805]
42. Bizzarro MJ, Dembry LM, Baltimore RS, Gallagher PG. Changing patterns in neonatal *Escherichia coli* sepsis and ampicillin resistance in the era of intrapartum antibiotic prophylaxis. *Pediatrics*. Apr; 2008 121(4):689–96. [PubMed: 18381532]
43. Shah P, Nathan E, Doherty D, Patole S. Prolonged exposure to antibiotics and its associations in extremely preterm neonates--the Western Australian experience. *Journal of Maternal-Fetal and Neonatal Medicine*. Nov; 2013 26(17):1710–4. [PubMed: 23565836]

44. Gomez R, Romero R, Nien JK, Medina L, Carstens M, Kim YM, Espinoza J, Chaiworapongsa T, Gonzalez R, Iams JD, Rojas I. Antibiotic administration to patients with preterm premature rupture of membranes does not eradicate intra-amniotic infection. *Journal of Maternal-Fetal and Neonatal Medicine*. Feb; 2007 20(2):167–73. [PubMed: 17437216]
45. Goldenberg RL, Mwatha A, Read JS, Adeniyi-Jones S, Sinkala M, Msmanga G, Martinson F, et al. The HPTN 024 study: The efficacy of antibiotics to prevent chorioamnionitis and preterm birth. *American Journal of Obstetrics and Gynecology*. Mar; 2006 194(3):650–61. [PubMed: 16522393]
46. Hopkins L, Smaill F. Antibiotic regimens for management of intraamniotic infection. *Cochrane Database Syst Rev*. 2002; (3):CD003254. *. [PubMed: 12137684]
47. Ugwumadu A, Reid F, Hay P, Manyonda I, Jeffrey I. Oral clindamycin and histologic chorioamnionitis in women with abnormal vaginal flora. *Obstetrics and Gynecology*. Apr; 2006 107(4):863–8. [PubMed: 16582124]
48. Kenyon SL, Taylor DJ, Tarnow-Mordi W, ORACLE Collaborative Group. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. *Lancet*. Mar 31; 2001 357(9261):979–88. ORACLE Collaborative Group. [PubMed: 11293640]
49. Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. *Cochrane Database Syst Rev*. Dec 2.2013 12:CD001058. *. [PubMed: 24297389]
50. American ACOG (American Congress of Obstetricians and Gynecologists) Committee on Obstetric Practice. ACOG Committee Opinion No. 485: Prevention of early-onset group B streptococcal disease in newborns. *Obstetrics and Gynecology*. Apr; 2011 117(4):1019–27. [PubMed: 21422882]
51. Verani JR, McGee L, Schrag SJ, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. *Morbidity and Mortality Weekly Report: Recommendations and Report*. Nov 19; 2010 59(RR-10):1–36.
52. Verani JR, Spina NL, Lynfield R, Schaffner W, Harrison LH, Holst A, Thomas S, et al. Early-onset group B streptococcal disease in the united states: Potential for further reduction. *Obstetrics and Gynecology*. Apr; 2014 123(4):828–37. [PubMed: 24785612]
53. Greenberg MB, Anderson BL, Schulkin J, Norton ME, Aziz N. A first look at chorioamnionitis management practice variation among US obstetricians. *Infectious Diseases in Obstetrics and Gynecology*. 2012; 2012:628362.
54. Czik MJ, McCarthy FP, Murphy KE. Chorioamnionitis: From pathogenesis to treatment. *Clinical Microbiology and Infection*. Sep; 2011 17(9):1304–11. [PubMed: 21672080]
55. Gonçalves LF, Chaiworapongsa T, Romero R. Intrauterine infection and prematurity. *Mental Retardation and Developmental Disabilities Research Reviews*. 2002; 8(1):3–13. [PubMed: 11921380]
56. ACOG (American Congress of Obstetricians and Gynecologists) Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 127: Management of preterm labor. *Obstetrics and Gynecology*. Jun; 2012 119(6):1308–17. [PubMed: 22617615]
57. Joram N, Launay E, Roze JC, Caillon J, Franco-Montoya ML, Bourbon J, Jarreau PH, Gras-Le Guen C. Betamethasone worsens chorioamnionitis-related lung development impairment in rabbits. *American Journal of Perinatology*. Sep; 2011 28(8):605–12. [PubMed: 21494996]
58. Been JV, Degraeuwe PL, Kramer BW, Zimmermann LJ. Antenatal steroids and neonatal outcome after chorioamnionitis: A meta-analysis. *BJOG : An International Journal of Obstetrics and Gynaecology*. 2011; 118(2):113–22. *. Jan. [PubMed: 21054759]
59. Van Dyke MK, Phares CR, Lynfield R, Thomas AR, Arnold KE, Craig AS, Mohle-Boetani J, et al. Evaluation of universal antenatal screening for group B streptococcus. *The New England Journal of Medicine*. 2009; 360(25):2626–36. Jun 18. [PubMed: 19535801]
60. Kim SY, Russell LB, Park J, Verani JR, Madhi SA, Cutland CL, Schrag SJ, Sinha A. Cost-effectiveness of a potential group B streptococcal vaccine program for pregnant women in South Africa. *Vaccine*. Apr 7; 2014 32(17):1954–63. 2014. [PubMed: 24530145]
61. Combs CA, Gravett M, Garite TJ, Hickok DE, Lapidus J, Porreco R, Rael J, et al. Amniotic fluid infection, inflammation, and colonization in preterm labor with intact membranes. *American Journal of Obstetrics and Gynecology*. 2014; 210(2):125.e1–15. Feb. [PubMed: 24274987]

62. Bastek JA, Weber AL, McShea MA, Ryan ME, Elovitz MA. Prenatal inflammation is associated with adverse neonatal outcomes. *American Journal of Obstetrics and Gynecology*. May; 2014 210(5):450.e1–10. 2013. [PubMed: 24361788]
63. Horowitz S, Horowitz J, Mazor M, Porath A, Glezerman M. *Ureaplasma urealyticum* cervical colonization as a marker for pregnancy complications. *International Journal of Gynaecology and Obstetrics*. Jan; 1995 48(1):15–9. [PubMed: 7698376]
64. Yoon BH, Romero R, Lim JH, Shim SS, Hong JS, Shim JY, Jun JK. The clinical significance of detecting *Ureaplasma urealyticum* by the polymerase chain reaction in the amniotic fluid of patients with preterm labor. *American Journal of Obstetrics and Gynecology*. Oct; 2003 189(4): 919–24. [PubMed: 14586326]
65. Genc MR, Ford CE. The clinical use of inflammatory markers during pregnancy. *Current Opinion in Obstetrics & Gynecology*. 22(2):116–21. 2010. Apr. [PubMed: 20139764]
66. Baker CJ, Carey VJ, Rench MA, Edwards MS, Hillier SL, Kasper DL, Platt R. Maternal antibody at delivery protects neonates from early onset group B streptococcal disease. *The Journal of Infectious Diseases*. Mar 1; 2014 209(5):781–8. [PubMed: 24133184]
67. Burns G, Plumb J. GBS public awareness, advocacy, and prevention--what's working, what's not and why we need a maternal GBS vaccine. *Vaccine*. 2013; 31(Suppl 4):D58–65. Aug 28. [PubMed: 23973348]
68. Le Doare K, Kampmann B. Breast milk and group B streptococcal infection: Vector of transmission or vehicle for protection? *Vaccine*. May 30; 2014 32(26):3128–3132. [PubMed: 24736004]
69. Dempsey AF, Pyrzanowski J, Donnelly M, Brewer S, Barnard J, Beaty BL, Mazzoni S, O'Leary ST. Acceptability of a hypothetical group B strep vaccine among pregnant and recently delivered women. *Vaccine*. 32(21):2463–8. 2014. May 1. [PubMed: 24662708]
70. Melin P, Efstratiou A. Group B streptococcal epidemiology and vaccine needs in developed countries. *Vaccine*. 2013; 31(Suppl 4):D31–42. Aug 28. [PubMed: 23973345]
71. Menon R, Taylor RN, Fortunato SJ. Chorioamnionitis--a complex pathophysiologic syndrome. *Placenta*. 2010; 31(2):113–20. Feb. [PubMed: 20031205]
72. Romero R, Miranda J, Chaiworapongsa T, Chaemsaihong P, Gotsch F, Dong Z, Ahmed AI, et al. A novel molecular microbiologic technique for the rapid diagnosis of microbial invasion of the amniotic cavity and intra-amniotic infection in preterm labor with intact membranes. *American Journal of Reproductive Immunology*. Apr; 2014 71(4):330–58. [PubMed: 24417618]
73. Oh KJ, Lee SE, Jung H, Kim G, Romero R, Yoon BH. Detection of ureaplasmas by the polymerase chain reaction in the amniotic fluid of patients with cervical insufficiency. *Journal of Perinatal Medicine*. May; 2010 38(3):261–8. [PubMed: 20192887]

Synopsis

Chorioamnionitis is the process of active infection within the amniotic cavity that induces an inflammatory response. Maternal intrauterine inflammation is the underlying mechanism of a significant portion of maternal and neonatal morbidity and mortality worldwide. It can be diagnosed based on a variety of both clinical and histopathological criteria, complicating its epidemiologic quantification and study. A wide variety of pathologic organisms can cause chorioamnionitis. Prompt diagnosis and timely treatment with broad-spectrum antibiotics can help avert the significant short-term (endometritis, neonatal sepsis and perinatal infections) and long-term consequences (infant's systemic and neurologic sequelae) that may result. This review aims to summarize the up-to-date diagnosis criteria, treatment protocols and long-term sequelae of missed diagnoses or poorly treated disease. It also calls for future studies which aim to better understand the mechanism of disease and to develop better detection and intervention methods to prevent the significant associated morbidity.

Key Points

Chorioamnionitis as a process of infection and inflammation that affects the fetus of a gravid mother that can cause significant morbidity.

Diagnosis of chorioamnionitis is based on a constellation of clinical, laboratory, and/or histopathologic findings, making strict evaluation of the condition challenging.

Chorioamnionitis is associated with many short-term and long-term neonatal morbidities that cause a significant burden of disease on society.

With timely diagnosis, broad antibiotic therapy to treat chorioamnionitis, either before delivery or shortly thereafter, can help minimize significant morbidity from the condition.

Cesarean delivery following chorioamnionitis does not improve perinatal outcomes compared to vaginal delivery.

Figure 1.

A diagram exhibiting the relationship between different diagnostic criteria of chorioamnionitis and neonatal outcomes.

Figure 2.

Incidence of early- and late-onset invasive group B streptococcal (GBS) disease --- Active Bacterial Core surveillance areas, 1990--2008, and activities for prevention of GBS disease. The United States and Western Europe are similar in terms of their prevalence of GBS. From Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. *MMWR Recomm Rep*. Nov 19 2010;59(RR-10):1-36; with permission.

Figure 3.

Algorithm for screening for group B streptococcal (GBS) colonization and use of intrapartum prophylaxis for women with preterm* labor (PTL).

* At <37 weeks and 0 days' gestation.

† If patient has undergone vaginal-rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. GBS-colonized women should receive intrapartum antibiotic prophylaxis. No antibiotics are indicated for GBS prophylaxis if a vaginal-rectal screen within 5 weeks was negative.

§ See [Figure 4](#) for recommended antibiotic regimens.

¶ Patient should be regularly assessed for progression to true labor; if the patient is considered not to be in true labor, discontinue GBS prophylaxis.

** If GBS culture results become available prior to delivery and are negative, then discontinue GBS prophylaxis.

†† Unless subsequent GBS culture prior to delivery is positive.

§§ A negative GBS screen is considered valid for 5 weeks. If a patient with a history of PTL is re-admitted with signs and symptoms of PTL and had a negative GBS screen >5 weeks prior, she should be rescreened and managed according to this algorithm at that time.

From Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. Nov 19 2010;59(RR-10):1-36; with permission.

Figure 4.

Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease.

Abbreviation: IV = intravenously.

* Broader spectrum agents, including an agent active against GBS, might be necessary for treatment of chorioamnionitis.

† Doses ranging from 2.5 to 3.0 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available to reduce the need for pharmacies to specially prepare doses.

§ Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cephalosporin are considered to be at high risk for anaphylaxis and should not receive penicillin, ampicillin, or cefazolin for GBS intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.

¶ If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testingshould be performed on prenatal GBS isolates from penicillin-allergic women at high

risk for anaphylaxis. If no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk for anaphylaxis.

** Resistance to erythromycin is often but not always associated with clindamycin resistance. If an isolate is resistant to erythromycin, it might have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and testing for inducible clindamycin resistance has been performed and is negative (no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

From Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. Nov 19 2010;59(RR-10):1-36; with permission.

Figure 5.

Algorithm for suggested management of chorioamnionitis with a viable fetus.

*Broad Spectrum antibiotics consideration may include Ampicillin, Gentamycin, Clindamycin, Flagyl, Erythromycin and Zosyn.

Figure 6.

Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns.

From Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. *MMWR Recomm Rep*. Nov 19 2010;59(RR-10):1-36; with permission.

* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC) including white blood cell differential and platelet counts, chest radiograph (if respiratory

abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

§ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

¶ Limited evaluation includes blood culture (at birth) and CBC with differential and platelets (at birth and/or at 6--12 hours of life).

** See Table 3 for indications for intrapartum GBS prophylaxis.

†† If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

§§ If 37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶ Some experts recommend a CBC with differential and platelets at age 6--12 hours.

Table 1

A summary of representative studies or meta-analyses, evaluating the relationship between chorioamnionitis and selected short-term neonatal outcomes GA=Gestational Age; VLBW= Very Low Birth Weight (<1,500 grams); OR=Odds Ratio.

Short Term Outcomes Following Chorioamnionitis					
Neonatal Condition	Study	Study Design	Chorioamnionitis criteria	Sample Size	OR, adjusted where available
Early Onset Sepsis	Sorashaim et al ²⁴	Retrospective Cohort (<29 weeks)	Histologic	N=384	5.54 (2.87-10.69)
Late Onset Sepsis	Strunk et al ³¹	Retrospective Cohort (<30 weeks)	Histologic	N=838	0.74 (0.57-0.96)
Peri-Intraventricular Hemorrhage	Sorashaim et al ²⁴	Retrospective Cohort (<29 weeks)	Histologic	N=384	1.62 (1.17-2.24)
Peri-ventricular Leukomalacia	Garcia-Munoz et al ²⁸	Retrospective Cohort (VLBW infants)	Clinical	N=451	24.62 (1.87-324.28) *
Necrotizing Enterocolitis	Been et al ³²	Meta-analysis	Clinical, Histological	7 studies N=5,889	1.24 (1.01-1.52)
Bronchopulmonary dysplasia	Hartling et al ³³	Meta-analysis	Clinical, Histologic	59 studies N=15,295	1.89 (1.56-2.3) (Adjusted for GA) 1.58 (1.11-2.24)
Retinopathy of Prematurity	Mitra et al ³⁴	Meta-analysis	Clinical, Histologic	27 studies N=10,590	1.33(1.14-1.55) Adjusted for GA 0.98 (0.77-1.26)

* Indicates Adjusted Relative Risk (rather than Odds Ratio)

Table 2

A summary of representative studies or meta-analyses evaluating the relationship between chorioamnionitis and selected short term neonatal outcomes OR=Odds Ratio

Long Term Outcomes Following Chorioamnionitis					
Neonatal Condition	Study	Study Design	Chorioamnionitis Criteria	Sample Size	OR (95% CI), adjusted where available
Low Cognitive Score	Pappas et al ³⁵	Retrospective Cohort	Both Histologic and Clinical Chorioamnionitis	N=1480	2.00 (1.10-3.64)
Lower Language Score	Pappas et al ³⁵	Retrospective Cohort	Both Histologic and Clinical Chorioamnionitis	N=1480	1.24 (0.83-1.84)
Cerebral Palsy	Shatrov et al ²⁷	Metanalysis	Clinical Chorioamnionitis	12 studies	2.41 (1.52-3.84)
Cerbral Palsy	Shatrov et al ²⁷	Metanalysis	Histologic Chorioamnionitis	8 studies	1.83 (1.17-2.89)
Neurodevelopmental Impairment	Rovira et al ³⁶	Prospective Cohort	Histologic Funisitis	N=144	4.07 (1.10-15.09)

Table 3

Indications and Non-indications for Intrapartum Antibiotic Prophylaxis to Prevent Early-Onset Group B Streptococcal Disease

Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis not Indicated
<p>Previous infant with invasive GBS disease GBS bacteriuria during any trimester of the current pregnancy</p> <p>Positive GBS screening culture during current pregnancy * (unless a cesarean delivery, is performed before onset of labor on a woman with intact amniotic membranes)</p> <p>Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following:</p> <ul style="list-style-type: none"> • Delivery at less than 37 weeks of gestation[†] • Amniotic membrane rupture greater than or equal to 18 hours • Intrapartum temperature greater than or equal to 100.4°F (greater than or equal to 38.0°C)[‡] • Intrapartum NAAT[§] positive for GBS 	<p>Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)</p> <p>GBS bacteriuria during previous pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)</p> <p>Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age</p> <p>Negative vaginal and rectal GBS screening culture result in late gestation * during the current pregnancy, regardless of intrapartum risk factors</p>

Abbreviation: NAAT = Nucleic acid amplification tests

¶ If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

** NAAT testing for GBS is optional and might not be available in all settings. If intrapartum NAAT is negative for GBS but any other intrapartum risk factor (delivery at <37 weeks' gestation, amniotic membrane rupture at 18 hours, or temperature 100.4°F [38.0°C]) is present, then intrapartum antibiotic prophylaxis is indicated.

From Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. Nov 19 2010;59(RR-10):1-36; with permission.

* Intrapartum antibiotic prophylaxis is not indicated in this circumstance if a cesarean delivery is performed before onset of labor on a woman with intact amniotic membranes.

[†]Optimal timing for prenatal GBS screening is at 35--37 weeks' gestation.

[§]Recommendations for the use of intrapartum antibiotics for prevention of early-onset GBS disease in the setting of threatened preterm delivery are presented in Figure 3.